Freireich, Emil J. 1997

Dr. Emil J. Freireich Oral History 1997

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National Cancer Institute Oral History Project

Interview with Emil J Freireich, M.D.

conducted on June 19, 1997, by Gretchen A. Case

in Dr. Freireich's offices at the University of Texas

M.D. Anderson Cancer Center

GC: The way I usually start out is asking people to give me kind of an overview of what happened to them before the NCI.

EF: Before NCI?

GC: Life before NCI.

EF: How much time do you want to devote to that?

GC: As much as you feel is important.

EF: I was born in 1927, so when I gave the festschrift [in 1977, celebrating Dr. Freireich's 70th birthday] talk, I said to myself, most people who live in the contemporary world are unable to perceive of the speed at which the world we live in changes. The only way you can do that is in terms of one human lifespan because everybody is living and they know that they were born. If they're 20, they know what 20 years is. If they're 50, they know what 50 years is. So I like to think of my background in that context.

I was born in 1927. Paul Ehrlich, who was the first person who ever conceived of using a chemical to treat a human disease, died in 1915. So if you think about our contemporary knowledge of the treatment of disease with chemicals, you see, it actually only spans a little more than one lifespan.

Nineteen-twenty-seven was an important date because, of course, it was two years before the Great Depression in the United States. So people born in that era are a special brand of people because they lived through one of the greatest economic dislocations in the history of our species—the Great Depression of 1929.

And during that period of time, when I was a young man of two—from 1930 to 1940 while the country was trying to recover from this event—I was living in the City of Chicago which, like all the inner cities during the Depression, were the most affected by the Great Depression. There was no work, no jobs, no money, and no food. So we have a generation of people who know what it is to be hungry, who know what it is to be isolated, because we didn't have any transportation, no means of getting around. So all people in America thought the world was within their little immediate vicinity. We didn't have cars and gas, and we didn't have horses and buggies either by that time.

So if you've seen "The King of Siam," we all grew up believing that the whole world was this jungle we were in. I have a good friend who was put in a concentration camp during the second World War when he was a young person. And you develop a mentality for survival—you develop a mentality which is not human. The humanness that people have derives from their ability to get outside of the essentials. As long as you're worried about food, shelter, safety, you're just like any other animal. And when you're in privation, that's what you are, you're animalistic. So were the people who grew up during the Depression, worried about food, shelter, safety. We used to get beat up, we used to get robbed, we used to steal, we were hungry, we did all kinds of things.

Family relationships were essentially nonexistent. My mother worked in a sweatshop. My father died when I was two. So you became a product of your environment. That's what transformed America, because all the immigrant cultures which tend to be clusters of people who depend on each other, were totally disrupted during the Great Depression. Now everybody was on their own. So that tells you a little bit about how you form your personality during those years.

Well, anyway, things got a little better by the thirties, as you know, and we began to get a little bit of food and some shelter, and some of us were actually able to go to high school. And I went to a high school when I was whatever age you are, twelve or so. And I attended an inner-city school called Tuley High School.

And we were beginning—to give you an idea, have you ever seen Kotter on TV?

GC: Yes.

EF: Well, that was my high school. The ghetto high school of today was the high school of the inner city during the Depression. And the idea is that what was going on in those things was a kind of a vocational rehabilitation program. My major was typing and shorthand, to give you an idea. I mean, we're now talking 1940—'37, '38, '40.

Academics, you know, reading and writing we barely got through. Typing and shorthand was important. And in this milieu, I just happened to make an acquaintance with a Kotter-type professor, a guy who had a reasonable background, who was intellectual, and who came into ghetto high schools to teach. And he taught physics. And for some reason I got interested in physics. He had a contest, and I did the contest.

This may be longer than you want it to be.

GC: No, that's fine.

EF: And I can remember—it's amazing, you're talking age thirteen, I'm seventy—when you have Alzheimer's, by the way, you remember ancient things better than recent things, as you know.

So my project was on the Bernoulli Principle. Do you know what the Bernoulli Principle is?

GC:I know I knew it at one point.

EF: It's what makes flight possible.

GC: Okay.

EF: It is the notion that the speed of the medium around any object determines the pressures on the surface. And the classic high school science project is you take a spigot and you run water under pressure so that you have a fountain and you put a ping-pong ball in it, and the ping-pong ball does not fall out of the fountain of water. And that's really amazing when you look at it. But when you think about it, that's the Bernoulli Principle. Because every time the ball moves to this side of the fountain, the speed of the motion of the water is more rapid on this side than it is on that side, and the force corrects it, so it stays in the center of the stream. That's the same principle that's used in flight. That's why you have a wing like this, because if this air flows faster than this air, that means the pressure is up. That's why airplanes fly.

So I got interested in the Bernoulli theory. I did this little science project, I won the prize, and my physics professor said, "Freireich, you ought to go to college." Well, we said, "What was college?"

GC: Oh, really?

EF:"Well," he said, "there is this place"—you've heard about the great land-grant colleges that were created during the Depression, the Big Ten? Illinois is one of the Big Ten colleges. And when we emerged from the Depression, some very smart social planners decided that some people might benefit from higher education.

And my professor, my schoolteacher—I can't remember his name—said, "You ought to go to college." So I said, "Okay. What do I need?" He said, "Well, you need a letter from me and you need twenty-five dollars because the Illinois Central Railroad goes from Chicago to Champaign-Urbana," blah, blah—what is it, about 125 miles?—"costs six dollars. Tuition for the first year costs six dollars. And we're going to give you six dollars for living and eating for the first month until you can make your way. So if you get twenty-five dollars, and you go to Champaign-Urbana on this date, you'll go to college."

So I went to my mother, who had just emerged—she married again—and I said, "I need twenty-five dollars." "Oh, okay." You know, that was like asking for a hundred thousand in 1938 or '39. But it turned out that she had friends in the community, and there was a, believe it or not, a Christian Scientist lady who had some money from an insurance policy from her husband who decided to do some good in the community. And my mother presented me to this lady, and they gave me twenty-five dollars.

And then I had a distant relative living in Peoria, and he donated a top coat because it got cold down there. And I got on the Illinois Central Railroad, and that was it.

GC: You just went on down?

EF: Down there. And I showed up—when I got off the train, I said, "Where's the university?" "It's over there." So I took the bus and went over there, and I said, "Where do you register for this school?" And they said, "You go over there." And I went over there, and this guy said, "What do you want to do?" I said, "Well, I never thought of that before." You know, I'd just wanted food, shelter, and safety.

GC: Right.

EF: But during the Depression, all children lived in the world of women. There were no men—they were all digging ditches and working on the WPA; there were no men. Occasionally you saw a man doing sewage cleaning or stuff like that, but you lived with women entirely. All the teachers were women. You spent all your time with women. So the men were all just—for boys, the masculine image was one of just slave labor. The women ran the place for the children. But there was one man I saw that I could really identify with. He was our family doctor. This guy was a doctor—*A Tree Grows in Brooklyn*—you've read that book?

GC: Yes.

EF: Well, this guy, *A Tree Grows in Brooklyn*, just one of those guys—during the Depression, he stayed in the community, he did general practice, he took care of anything and everything, and he was paid with food and kindness and that's it—a lovely guy. And whenever I got sick, Dr. Rosenbloom came to my house and he told my mother what to do: give me ice cream for my sore throat, and all that stuff. And I thought he was wonderful.

So when the guy said this to me, "What do you want to do?" I said, "Well, I want to be a doctor,"—like Dr. Rosenbloom. He said, "Okay. You have to take pre-med. Here's your courses." I think today you can take anything, English Literature, but in those days you had to take German—because the entire literature between the wars in medicine were in German; modern medicine in the world began in Germany—you had to take Chemistry I, and so on and so forth. "Okay." "Six dollars. Thank you. There's only one problem." "What is it?" "We don't have your transcript from your high school. What high school did you go to?" "I went to Tuley High School." He said, "Tuley High School. We've never had anyone from Tuley High School. But maybe they just didn't know how to do it. But I'll take care of it. We'll register you temporarily and I'll get your transcript." So they did. They had to call Tuley High School, and they figured out they had to send that I'd graduated.

And then the rest of the story is history. I got a job in a sorority cleaning floors that paid me six dollars a month. My room was six dollars a month, and I got free food for waiting tables during the week.

So then the problem was you have to have books and cigarettes and stuff like that. So I went back to my advisor and I said, "I'm broke." He said, "No problem. You have to get a scholarship." I said, "Good. How do you get a scholarship?" He said, "You get all A's." I said, "Okay." I worked very hard, I got all A's, and I got a scholarship from a fund called the Cook County Fund. And what the scholarship did was buy my books, give me X dollars for supplies, and paid my tuition. So now I was <u>loaded</u> rich.

GC: Right.

EF: Now, this is still during the war, remember, and I was under eighteen. So I'm all set. I'm on my way to fame and glory. And then I got to be eighteen, and you get drafted. So I got my notice for induction—I'd been about one year in school.

This is fun for me, but it's probably boring for you. Is it?

GC: Not at all! It's very interesting.

EF: Well, don't put it in the history. But anyway, I'll give you a little background because people always think I'm irascible, and there's always a reason for things like that.

But being drafted is one of the most humiliating experiences anyone can have, you see, because you walk in a room with a bunch of eighteen-year-old guys and take off all your clothes and stand there—it's like a concentration camp, you know, you stand there naked all day while people poke in your ears and hang on your head. And then at the end of the line, while you're all standing there naked, they say, "Has anyone ever had any illnesses?" I put my hand up because I was stupid. They said, "What did you do?" I said, "Well, I had a broken leg. I had to wear a cast." When I was in high school I played basketball. "Step over here."

I came into a room—they had us lined up and then you come into this room—you're still naked, now sitting on your bare butt, and you see a guy who comes straight out of "M*A*S*H"—slovenly uniform, cigarette hanging out of his mouth, ashes falling, hair in a mess, looks like he wants to kill people—this is the doctor I'm going to see. He says, "What's wrong with you!" I said, "Nothing wrong with me, sir."

You know, during the war, it was exciting to serve in the military because that was something every American did. We hated Japs, we hated Germans. "There's nothing wrong with me. I'm healthy, sir." He said, "What is all this about your leg?" I said, "Well, I had this—it was nothing—I had basketball, and wore a cast." And while he was examining me he was foul-mouthing the war and the military, "This is the stupidest thing, people kill everybody, there's no reason for it, we're not getting anywhere, the world's going to"—he was one of these M*A*S*H guys.

So I'd never heard anything like that. I go to the movies. This is Americans charging against the Japs. "Okay, put your clothes on, you're going out." I walked out the door and the guy goes [imitates noise of an official stamp], "4-F." 4-F meant you were deferred for medical reasons. Now this is for an eighteen-year-old the world's greatest humiliation. There's nothing worse than being a 4-F because those are the draft-dodgers that won't serve their country and such. This was a really humiliating experience.

So I went home and talked to my family. I didn't know what to do. So they said, "You've got to go back to school." So back on the Illinois Central, I went back to school. And I got all A's.

Well, during the war, all the universities in the country accelerated education because we had to get—you know, like we did for the war effort. We had to have people who were doctors, lawyers, engineers, so we had—undergraduate school became a three-semester process, so you did a year and a half in every year. Secondly, the pre-medical curriculum for medical school was reduced from three semester hour years to two. So that by the time you went for fifteen months, you were eligible for medical school.

I was seventeen, and my third year my professor said, "If you want to go to medical school, you've got to apply to go to medical school." "How do you do this?" "You fill in the form." I filled in the form. I got a letter that said, "You're accepted to medical school."

I said, "Wait a minute! Why should I go to medical—I don't want to go back to Chicago; I'm in Champaign, Illinois, having a good time, I have these girls, I have cigarettes, I've got a nice house"—a beautiful place.

Have you ever been to Champaign, Illinois?

GC: No, I haven't.

EF:A beautiful town, college town like Austin. They're beautiful towns—a beautiful town, beautiful campus, with young people having a good time. "Why do I want to go to Chicago and beat my head off?"

Well, I was living in an independent house with a lot of people, several of whom wanted to be doctors, and they didn't get in, and I did, and they all said, "Freireich, you're crazy if you turn it down." So I said, "Okay, I'll go to medical school," against my wishes.

So now we're at 1944. I'm seventeen—is that right?—yes, seventeen years old. I had to be more than that. Let's make it '45. I must have been eighteen because I went through that draft business.

Well, anyway, I'm very young and I go to medical school in Chicago. How do you go to medical school? Well, now we've got several problems. Medical school is not six dollars a semester; it's a thousand. Today it's twenty-five thousand. Plus you have to have a microscope. So that's out of the question. So I can't go to medical school.

So I go to the William Cook Foundation. What do you do? "Well, you're 4-F. There is a program in the State of Illinois for rehabilitation of disabled people."

I had a roommate who had a severe disability. He was, "You ought to apply." So I applied. The guy came out and he examined me. I get a letter, "You're supported by the rehabilitation institute, and what they will do is they buy all your equipment and pay your tuition." To medical school! Now all I've got to do is live.

So I went to my poor starving mother and I said, "You're going to have to take me back." So she put me up for the next four years.

Now, medical schools were also accelerated. They did the same thing; you did a year and a half every year. And the medical schools were committed to the military. They had ASTP (Army) and V-12 (Navy) programs so that the military could create doctors to go out there and patch up all these guys who are getting blown up by the Japs.

So when I entered medical school, you needed eight semesters, so in two and a half years you would be a doctor. So, okay, it takes fifteen months here, and it takes thirty months here, so in forty-five months, you're an M.D.

But fortunately for me, the war cooled down in 1945, as you recall, and they switched back to a four-year medical school. So I actually went to medical school for four years, where I graduated in 1949. So instead of being twenty, I was twenty-two, which was great. Now I'm an old man.

[Laughter]

EF: At medical school I did very well. I graduated sixth in a class of 180. I wasn't outstanding, I was just okay. And then you had to decide on your internship. So I said, "Well, I want to be family doctor, so I'm going to go to the best family doctor program," which was Cook County Hospital. Cook County Hospital was the city/county hospital in Chicago.

Are you running out of tape?

GC: No, I'm just watching the voice level. You're okay.

EF: Should I shorten it a little bit?

GC: No, no, you're fine.

EF:I haven't even gotten to NIH yet.

GC: No, I want you to keep going. I just wanted to make sure that your voice was picking up.

EF: Well, Cook County Hospital in 1949 was the prototypic city/county hospital of the inner city. In Chicago it was an entirely Southern black hospital. What happened after the war was, of course, a lot of blacks were caught in the South working agricultural menial jobs—there was still lots of segregation in 1949—there were no jobs in the northeastern cities. So they used to work this stuff until they got sick. When they got sick, their owners—employers in those days—put them on that Illinois Central for six dollars, go to Chicago and get taken care of at Cook County Hospital.

So we had the dregs of humanity. If you go to India, the inner ghetto, that was Cook County Hospital. You had people who had never had any healthcare, were malnourished, uneducated, can't speak English, they have syphilis, gonorrhea, hepatitis, trauma, stab each other, kill each other, shooting wounds. I spent a month on our emergency room. The police used to drag in people who'd just get slaughtered on the streets, drug addicts, scum of the earth.

So that was a very interesting experience because, for instance, you did everything, so I did OB. And in obstetrics in one month I attended the delivery of a hundred babies, in one month!

GC: Wow!

EF: And I was the only one in attendance. I'd never seen a mother deliver a baby.

[Laughter]

EF: Not only that, but when the residents came around, they said, "Do you want to learn how to do forceps?" We said, "Sure." "Well, here's a patient. Let's do forceps." It was really ugly stuff.

Medicine at Cook County Hospital was impersonal, simply because of the social setting in which it was practiced. And although I came from a background of that, as I went through medical school I began to have higher and higher principles; you know, they kept talking about doctors and—*A Tree Grows in Brooklyn*, remember.

So I didn't like the way this went on, so I had major confrontations with the administration and literally I was fired because I didn't like the way they did things.

I had signed up for a two-year internship in family practice. And after a year I was fired, but I had a contract, and they told me I couldn't leave unless I found someone to take my place. So I spent six months trying to find some poor innocent graduate who couldn't get a job anywhere else who would fill my six-month term, and I did. And I left after eighteen months. And the question was should I go into practice or not? I had my license. I had nothing wrong with that.

I kind of felt like—I knew how to deliver babies and fix hernias and do hemorrhoids, and, you know, I was ready to be *A Tree Grows in Brooklyn*. But the one thing that bothered me was that internal medicine was very complicated: heart failure, blood diseases, digitalis, morphine—I just felt like I didn't know enough about that.

And so I had an opportunity to go to the Presbyterian Hospital of Chicago, across the street, which was then chaired by a young, brilliant internist who had done research in Boston and was attracted to the Presbyterian Hospital. Well, that was the Rush Medical Clinic. You may have heard of the Rush Clinic. It was a very famous place. It's where Dr. Sippy did the ulcer diet, where Roland Woodyatt worked on diabetes. They were a bunch of very famous people.

But after the war, when the modern medicine grew up on the East Coast, particularly in Boston, Chicago was a little out of it. So they wanted to upgrade the quality of their science. They recruited Howard Armstrong.

So I went across the street, and I said, "Dr. Armstrong, I've been inspired by your rounds that you give at Illinois and County Hospital, and I want to learn internal medicine because I want to be a family doctor, but I don't understand medicine, it's too complicated. You know, I can do operations—all the ones you need to do; I can't do big ones." And I did ENT and I did ophthalmology, I knew all that stuff. But I didn't know much about medicine, too complicated. "Good idea. Why don't you do a year of internal medicine." So I signed up for a year of internal medicine.

Well, that began on a very bad track because internal medicine, of course, is very academic and very intellectual. You begin to think about—you know, in 1949, surgery was, you know, it's pretty obvious what to do; if you've got a lump, take it out; you cut, you tie blood vessels, and stuff like that; babies, pretty obvious.

Medicine was very pragmatic. But medicine was becoming physiology. People were beginning to ask about the mechanisms of disease: "Why do people get sick? How do they get sick? What are these organisms? Can we treat disease?" It's amazing to realize that the idea that we can treat disease with chemicals just began one lifetime ago—don't forget—so we're now in 1949.

Now, during the war there were a number of exciting developments, as you know: the malaria thing was controlled during the war. That was the beginning of NIH. Antibiotics were discovered by Dr. Fleming in England, by [Gerhard] Domagk in Germany. But it was in America where antibiotics were developed by the American pharmaceutical industry. We had penicillin.

So when I was an intern, to give you an idea of the magnitude of change in medicine, I spent one month in the largest hospital in the Cook County complex, which was the tuberculosis hospital. Eighty-five percent of the population in the City of Chicago was tuberculin-positive, meaning they were clearly exposed to TB.

GC: Eighty-five percent?

EF: Yes. That was the state of our knowledge of tuberculosis. Our infectious disease hospital major problem was polio myelitis, paralytic polio. Children were dying by the thousands in these iron lungs, couldn't breathe.

So internal medicine was a real eye-opener for me. I mean, we began to talk about gastric acid, we began to talk about hypertension. Oglesby Paul who was there was an expert in electrocardiography—we began to talk about arrhythmias. And the man who described—do you know what the leading cause of death in the western world is today? It's coronary artery disease. The man who first described a heart attack was one of my professors, James B. Herrick.

GC: Oh, really?

EF: Yes. So it just tells you how contemporary our knowledge is. Prior to his description, when he was a young man at Presbyterian Hospital, the association between an infarct in the heart and the event of pain in the chest and dying suddenly, no one understood why people just dropped over dead. That shows you how contemporary our knowledge was.

Diabetes, there was no insulin. Roland Woodyatt was one of the pioneers in first applying insulin. He was the first person to recognize that sugar in the diet affected the life of diabetics, whether they had coma or not. And he had patients on what is now still called the Woodyatt diet, where you replace carbohydrates with sugars. So these were my professors.

So Western medicine was there, and it was very exciting to me. And we went along for about a year. I became Chief Medical Resident. I really liked what I was doing.

And then Dr. Armstrong got fired. And the reason that he got fired was that all the house staff gravitated to him, away from the conventional attendings. And they organized a revolt, and he was fired.

And when he got fired, he called me in and said, "Freireich, you're too smart for these guys because you know all that old stuff. You have to learn the modern physiology medicine began in Boston by Soma Weiss. You have to go to Boston." "Yes, sir." I mean, in those days, we were respectful. You didn't say anything to your professor.

So I had a broken down Oldsmobile, and I put everything I owned in the back of the car and I drove to Boston. Dr. Armstrong gave me three letters. He said, "What do you want to study in medicine?" I said, "Well, I just want to be a family doctor, Dr. Armstrong." He said, "Well, what do you know the least about?" I said, "I know the least about hematology," because we had a broken down old hematologist who didn't know much. And he said, "Okay. Go do a year of hematology fellowship and research in Boston," and he gave me the names of the three names of the greatest hematologists in Boston: Bill Dameshek, who was the founder of the *Journal of Blood*, one of the most famous people in his field; Joe Ross, who was one of the first to use radioisotopes, after the war when they learned from the atomic effort that you could make isotopes which were then detectible by counters and we could study physiology—turnover, it was the first idea we had, that when you had albumin in the blood, it wasn't made to stay there, and it was constantly being used and replaced, and all that turnover data began just in—all that research was just beginning in 1953.

And the third one was Franz Alexander, who was a person interested in blood coagulation, which is very fundamental, as you know, to everything.

So I went to Boston, and I interviewed these three people, and they all offered me a job because I had a letter from Dr. Armstrong and they all thought he was great. So it was a tough decision where to go.

Well, it turned out all tough decisions are easy. The reason it turned out to be easy is because Dr. Ross had a young man working in his lab named Stuart C. Finch, and Stu Finch had written a grant to study the anemia of rheumatoid arthritis. And he needed a young guy to do that work, and for this I would get paid $3,000.

Dr. Dameshek had no money. I had to do it for free. Dr. Alexander had no money. So I worked for Dr. Ross because I had $3,000.

Shortly after that, a nurse that I'd been dating in Chicago came to town, and it's a long story, and we got married in Boston and had our first baby.

And I worked on the physiology of red cells for two and a half years at the Mass Memorial Hospital. Now the person who was the Dean of this institution, Boston University Medical School, was a man named Chester Scott Keefer. And if your history is any good, you'll realize that when Eisenhower was President, 1952, I guess it was, he amalgamated the Departments of Health, Education, and Welfare, and made a new Department. And the first Secretary was Oveta Culp Hobby, amazingly from Houston. And Oveta Culp Hobby was a newspaper publisher, and she didn't know anything about health, so she created the position Undersecretary for Health, which still exists today.

And the first person to hold that position was Dr. Keefer. And the reason Dr. Keefer was chosen was Dr. Keefer was really an unspeakably brilliant man. I mean, he was—if you think Armstrong was brilliant, Dr. Keefer is an unbelievably brilliant guy. He knew everything about everything. He taught third-year students up until the day he died.

He was the chairman of the development of the penicillin program in the military. He was an infectious disease expert, and very well known. And for that reason, he was chosen.

But he decided he wouldn't give up his true love, Boston University; he had to stay there. So he did two jobs. He had three days in Washington, four days, including the weekend, in Boston. He commuted regularly every week—something I'm planning to do, actually—and he had a hotline on his phone, so he could do both jobs from both locations.

And I was going along very well in my career at Boston University. It looked like I'd been . . . made a Member of the American Federation of Clinical Research, I'd given an abstract, I'd discovered something—I'd really discovered something important, as a Fellow, and it was something fundamental about the physiology of iron in inflammatory conditions. And the world's authority, Dr. Max Wintrobe, had published something like 23 papers on the biology of the anemia infection, and Freireich, out of the blue, totally turned this field around. And in the context of 1953 to 1997, forty-plus years, what I discovered has been true and is still the basis of the understanding of hemoglobin metabolism.

And I mention that because Wintrobe wrote the first comprehensive textbook of medicine, clinical hematology, he's world-famous, he ended up in Salt Lake City, and he and I were intellectual opposites on this issue. Dr. Ross supported me, and I got my work published, and it turned out to be true.

The reason that's important is that if you begin in a career of research, the most important thing—and this has been studied systematically—it is when you look at Nobel laureates and people who are successful, you always find one characteristic: that is, when they started out, they undertook a bold project, difficult, and they succeeded.

If you undertake a minor project and you succeed, it doesn't have any impact. You take a bold project and fail, it discourages you. But if you take something bold and succeed, that makes you bold. Now you can take the failures.

So I was lucky in that regard. It was brilliant work, actually, when you think about it in retrospect, without being self-serving. But it turned out to be very true and very important.

So I was headed for a great career in Boston. Everything was going fine. I would have moved up to a faculty position. And now we're in 1953, and I get a letter from the Army. I had been 4-F as a civilian, but since I was a physician—the doctor's draft—unconstitutional, immoral, illegal—it said that once you become a doctor, you're 1-A because now you can serve as a physician no matter how disabled you are—clearly discriminatory.

But I was 1-A, and then because I was working with Dr. Ross and we were using isotopes and doing important research for the Atomic Energy Commission, I was deferred. But in 1953, several senators introduced a bill that would eliminate the doctor draft because it clearly was unconstitutional. Basically, during the war you can do all kinds of silly things; you know, you can put Japanese in concentration camps, and so on, and you can draft doctors because of their profession. But after the war, people began to say, this isn't right, the military ought to train its own physicians. But the Army panicked because they saw a window there where they wouldn't have any doctors, so every eligible physician in the country was drafted.

Now, the idea was, of course, that they'd have all these people drafted, some of them would serve, some of them wouldn't serve, but they would play with this pool for the years until the military could come up with their flow of doctors. So I was drafted. And the deal was, you either accept the commission as a physician voluntarily, as a second lieutenant, or the law allowed them to draft you as a private, and then you go to boot camp. So, of course, everybody volunteered. So I volunteered, I was going to be a doctor.

I told Dr. Ross that I had to finish my research very quickly because I had to report for active duty in, oh, three months. I told my pregnant wife. We were ready to go.

One day I got a call from the secretary who said, "Dr. Keefer wants to see you." Dr. Keefer wants to see me! You know, that's like having a call from the gods! "Freireich!" "Yes, sir!" "Dr. Ross tells me you're doing a good job." "Oh, thank you, sir, I'm very pleased." "He also told me you got drafted in the Army." "Yes, sir. I have to leave in three months." "Have you ever heard of a place called the National Institutes of Health?" "No, sir." He says, "Well, there is this place down there, and I'm in charge of getting doctors to work down there, and I think you'd be wasting your career in peace time going to go in the Army. I want you to join the Public Health Service and go to NIH." "Yes, sir! How do I do it?" "You go down there tomorrow." He picked up his phone and called Washington—"Fred? I've got a young doctor here, his name is Freireich, let's see how you spell it, F-r- . . .—He'll be down there tomorrow morning. See what you can do." "You go down there and see Fred, and he'll tell you what to do." "Yes, sir." I went out and told my wife, "I've got to go to Washington." I jumped in my car—no, I took the bus. I took the bus to Washington. I took a bus from the bus station. I go to the HEW building.

Have you seen the HEW building? You know where it is?

GC: Yes.

EF: It's a big, impressive place. I go see Fred. "Dr. Keefer says you should go to NIH. Do you know where the NIH is?" "No, sir." "NIH is out here in Bethesda, but you're lucky, we have a car that goes up and back there. It leaves in ten minutes. You get on this car, you go out there to that big building, and you see what they want to do with you." "Yes, sir."

I get up, I go downstairs, wait a half hour, get on this bus going to the NIH campus. Well, you see, the Clinical Center had only been open for about a year, with this huge building, a bunch of little buildings, but a beautiful campus, <u>way</u> out in the country—I thought I was lost.

So I get off—the bus drops you off—I go up to that building there, "Yes, sir," go to the information desk, "Yes, sir." They made appointments for me with the Clinical Directors of the six institutes. So I went around and saw all of the institutes' directors. The guy in Allergy and Infectious Disease said, "We have a hematology program. It's run by Frank Ebaugh." I knew Frank Ebaugh. "And we've got a lot of guys, and there's an opportunity, and maybe you can get a lab," and this and that. And then I went to the Heart Institute.

I came to the Cancer Institute, and there was Gordon Zubrod. I walked in the front door—you've got to be careful about this because I'm telling you the truth; I'm not sure he told you the truth—so I walked into his office. "Freireich?" "Yes, sir." "Do you know anything about leukemia?" "Oh, yes, sir! I mean, I"—I didn't know anything about leukemia.

[Laughter]

EF:I did do a hematology residence, and leukemia patients who came were my responsibility. At that time the only thing we knew to do for leukemia patients was we gave them corticosteroids and methotrexate, and it sometimes lowered their counts, but they all died. And we didn't have any control for infection or platelets. Occasionally we could get some penicillin.

But I did study—all the leukemia patients were my responsibility. So I went out and talked to them and saw what happened to them. So I did understand a little bit. So I wasn't totally lying—because I was a hematologist by training. I'd been there for eighteen months, and I was going to be appointed in the Hematology Department. So I actually had credentials.

So I said, "Yes, sir, I know about leukemia." He said, "You know? I think what we're going to do here is work on chemotherapy for cancer. And from what I've been reading"—see, Zubrod came out of the pharmacology business: infectious disease, Hopkins, and St. Louis University. Well, he told you all that.

So when he came to town, he looked at what cancer was all about and he decided, you know, they need to do what they did in malaria for cancer, and that's start doing some chemotherapy. And from what he read, he thought leukemia would be an important target, so he wanted a hematologist.

So he said, "I think I would like you to start a leukemia program here." "Okay." "So you're hired." "Yes, sir."

I got in my car and went back to work, went to the lab, trying to finish up all my research—I had three important papers I was working on. I had lots of counts to do. You see, in those days you didn't have technicians—I had to do everything.

Forty-eight hours later I get a wire from the Defense Department, "Report for active duty in 48 hours." Whoa! So I called, and I said, "Listen, I have to have an extension. That's impossible. I've got a thing, a wife, children." "No, you can't do it." "Why?" Because the deal that the Army had with the Public Health Service is if the Public Health Service stole Army officers, they had to be on active duty before the Army knew about it. Otherwise, the personnel directors would fight with each other.

So the PHS guy said, "Freireich, you must be here in 48 hours, and you must be on active duty. Otherwise, the Army is going to get you."

So I went home and I told my lovely wife of 44 years now—she was, let's see—my son was born in July, and this was April, so she was six months pregnant. She's a very little thing. And we had a baby who was 15, 16 months old.

GC:I'm going to stop you for just a minute.

[End Side A, Tape 1]

[Begin Side B, Tape 1]

EF: We have to get to NIH. We're finally getting here.

GC: Yes. So you were talking to your wife about this 48-hour . . .

EF: And we didn't have any money. So we told our landlord that we were getting drafted. There was nothing he could do about the rent. And we put everything we owned in this car. It was a fast-back 1946 Oldsmobile, a very small car. We had a crib that we took apart and put in the back seat. My wife and I, we put all our luggage in the trunk and on the roof—everything we owned in this car.

Did you ever see the sharecroppers going—that was us.

[Laughter]

GC: With the chairs on top of everything?

[Laughter]

EF: Leaving Boston, going to Washington. Well, it's only 300 or 400 miles, something like that. It was a rough trip. We pulled into Washington April 8th. What do you do? I have to go to this place I was before, to the Clinical Center. With my car and everything, we drove to the front of the Clinical Center. "Deanie,"—it wasn't that hot in April—"you have to wait here. I have to go report for active duty." She waited in the car.

I went up to see Zubrod. He was doing something. In ten or fifteen minutes, "Freireich." "Yes, sir, reporting for active duty." "Great! Have you got a place to live?" "No." "What do you mean? You don't have a place to live?" "Well, we just arrived. We only had 48 hours." "Oh!" he said, "Well, don't worry about all that military stuff. This is the NIH. Find a place to live, and come to work when you're settled, maybe tomorrow."

So I went back down to my wife—no, I said to the secretary, "Well, how do I find a place to live?" Well, the NIH was out in the country, so they had a personnel office that helped you locate [a place to live]. So I went down there, and they gave me a list of people who would take you in a room. And we got back in the car and we drove around. We found a room in a house where we could take our two kids, and we were moved in.

The next day we had to find a regular place to stay because we couldn't stay in this rooming person's home for a year. So we spent the day looking around. We found a basement apartment that we could rent—we still don't have any money—and we rented that, and we moved.

And then the next day I went to work. "Reporting for active duty, Dr. Zubrod." "Oh, Freireich, yes. Well, we got you an office up on the twelfth floor." He was on the tenth floor. Have you been to the Clinical Center?

GC:I haven't been in it. I know where it is.

EF: So, you know, the way it was in the beginning, the concept was that the hospital was here, and there were supporting facilities, the doctors' offices and laboratories were here, so the idea was to make a connection between the research work and the clinical work.

So he was on the tenth floor in a fancy office. "Your office is on the twelfth floor." Okay. I go to the twelfth floor—you may have heard this story. Did you talk to Frei?

GC: Yes, I did, but I haven't heard this story.

EF: Well, this is true. He probably told you this story because he tells everybody. I walked up, I was looking at the names on the doors. It was rows of rooms. Twelve—said, Emil Frei III. "Damn! It's government typical—government stuff—can't even spell my name!" So I walk into this room. And here's this tall, skinny guy with no hair.

So I said, "Sir! Dr. Zubrod told me this was my office. You're in my office." He said, "Are you kidding? This is my office! What's your name?" So that's how Frei and Freireich met the first time.

[Laughter]

EF: He said, "You got the wrong room number. You're next door." It actually was next door. There was Emil Frei III—the first time we ever met each other—and Emil Freireich. And we have been friends from April 10, 1955 to this day—friends and intellectual colleagues, intellectual collaborators. I have very high regard for Emil Frei III, and we really fought the wars there in the Clinical Center.

So, anyway, I met Frei and he told me about his situation. He'd been there—when did he come? maybe February—he'd only been there three or four months. And they were struggling to get the service going. And I told him I was going to do leukemia. He said, "Oh, fine. Go see"—this is actually a true story.

Are you going to interview a guy named John Fahey?

GC: John Fahey?

EF: Yes.

GC:I haven't heard that name yet.

EF: Well, John Fahey was a clinical associate at that time. He's still a professor at UCLA School of Medicine. A clinical associate was a person who did a military two-year stint and then left.

And the other person I saw—this is in the first two days—was a guy named Jesse Steinfeld. Are you going to see him?

GC:I have his name down, too, yes.

EF: Well, Jesse was in the same boat, he was another one of these clinical associate guys. So they had been there for about a year, but of course I was a big authority because I was an officer, I was a regular staff person, I wasn't a trainee—these people were. And John Fahey said, "You're interested in leukemia. That's great! You know Jim Holland was here." Is Jim Holland on your list?

GC: Yes, he is.

EF:"Jim Holland was here, and he left, and he had these children with leukemia, two or three children with leukemia, and I was taking care of them—I don't know anything about it, I can barely handle it. Why don't you take these patients?" So day one I had two children with leukemia, day one, John Fahey gave me two children.

And Tom Frei said, "You're the hematologist, so you take care of the leukemia and I'll do the solid tumor work." That was Zubrod's interest.

And that was the beginning of the NCI thing. That's the background. So now you can ask me questions about the Clinical Center. Now I'm there, forever—for ten years.

GC: Okay. What did you arrive to? The Clinical Center was just being set up. How—

EF: The Clinical Center was—this was an amazing event. First of all, I came from Mass Memorial. It was an old medical school in Boston, and everybody is on everybody's head, and there's no money and no space, inner-city, hard to get around, snow, rain—so you come to Washington. The first thing that really struck us was that we were in a Southern town; everything was segregated. Department stores: black bathrooms, white bathrooms. It's hard to imagine—1955. Everything was segregated, there were no blacks anywhere.

And that shocked us because we were—you know, in Chicago there were race wars, but it was dominated—a huge black population, and they were all over the place. And Boston, of course, was where the Reconstruction began. You know, Boston is very anti-bias, so there wasn't any bias in Massachusetts. But Washington, you were in a Southern town. That was our first exposure to the South, and amazing, particularly in Virginia.

The second thing that was obvious was that we were out in the middle of nowhere with this huge hospital, which was essentially empty. I mean, they had—I've forgotten how many beds they had—250 or 300 beds. But it was essentially empty. As far as the Cancer Institute was concerned, there were two or three people on a ward, way overstaffed, nurses galore, psychologists, statisticians—everybody was there.

But the thing that impressed me the most about the place was, I decided to do research in my laboratory because I'd done research at Boston U., with isotopes. And I went to the administrative guy, and I said, "I need equipment." He said, "No problem. You go down to this room at the end of the hall, and just pick what you want!"

[Laughter]

EF: They had a room full of equipment that you would die for—radioactive counters, spectrophotometers, highly high-quality balances. Because in the planning, the Congress had set aside money for equipment, and you know how the government works, if you don't spend the money by the end of the fiscal year, it goes back. So they just bought everything in the science book. And there was—everything was there. This was Hansel and Gretel in the cookie house.

[Laughter]

EF:I mean, you could do anything. That really impressed me. So I want this and this, and I had a better equipped laboratory in three days than I had at Boston University in two years. That was one thing that impressed me.

The second thing that impressed me was the environment there was amazingly different from a university. There were no students. There was no teaching to speak of. There was no service work. You didn't have to go to clinic Monday, Wednesday, and Friday, and see thirty people.

And I've often said—it's an environment we tried to create around here when I was head of the department, the one we started here. You say to a young person, "Look, you're educated, you know a little bit of what's known, but your job is to figure out what's not known. So you decide what you want to do. Pick your problem, pick your equipment, just use your imagination, get at it." It's a terrific thing, terrific thing!

It's an environment that we need to create for young people because our educational system, as you know, is regimenting, not mind-expanding. So I'd spent all my life being told what I should do next. And I came to the NIH and people said, "Do what you want." And Zubrod started it off. "Reporting for active duty." "Well, don't worry about it, Freireich. Come back when you get your house." You could work twenty-four hours a day or one hour a day. You could work on leukemia, or you could work on breast cancer, or you don't have to work on anything. You can work on rheumatoid arthritis. It's amazing!

I was an opportunity to create your own challenges. I didn't have to go to clinic three afternoons a week. I didn't have to teach students Monday, Thursday, Friday. You know, just do what you want. So that's what happened.

But fortunately, we had inspiring leadership. In a situation where you can do what you want, you can do nothing, or you can get organized. So we got organized. We had inspiring leadership. To his credit, Gordon Zubrod was the inspiring leadership. And he decided that our agenda should be to apply clinical trial techniques that had just been developed in 1948 to the study of cancer. We had to know something about the natural history of cancer. We had to know something quantitative about the treatments that were being practiced, so to speak, in an empirical way.

And so we set about to talk to some of our colleagues. You see, there was a basic science establishment in place, but no hospital. So they brought in young doctors, and they said, "Okay, what are you going to do?" "Well, I can do anything." "Well, let's find out a little bit about what's known about cancer."

So we went around and talked to people who were working on cancer as a problem in the Cancer Institute. And the people who were our big influences—you may have heard these names before—were Lloyd Law and Abe Goldin. And these two people—Lloyd Law was the person who first developed the transplantable tumors in mice. And Abe Goldin was one of the people who first began to study the effect of chemicals on the natural history of these transplanted tumors.

And Mike Potter—you may meet him—who was working with Lloyd Law and was interested in immunoglobulins. And John Fahey actually worked with Mike Potter. He's the world's authority on immunoglobulins, John Fahey at UCLA. I still see him at meetings there once in a while.

The biggest honor I've gotten in my whole life was that was the first Outstanding Alumnus Award from NIH. And one of the things that Nancy Brun did, was she dug up some old pictures of the people who worked at the Clinical Center. The first one below the thing—[indicates pictures on wall]—is roughly 1956, '57, early in our career, and the last one is late in the career, about '64. And if you just look at the people who are on that list, it's a rogue's gallery of leadership in cancer research in the United States.

Because what came out of that environment was, one, attracting people who were adventurous, because you don't do what I did if you're not adventurous. I could have gone into the military and been a captain and gone into practice. But, you know, this looked like a challenge, so off we went to this place to do what we could do. And that was the people who were attracted there during that period of time.

And, secondly, they were given literally unlimited resources to do what their brains told them should be done. So we were in this thing, we talked to these basic science people, we began to formulate hypotheses for a clinical study, and we organized formal protocols, we devised criteria for response. Those were published—there was a lot of controversy about what we were doing.

And in ten years, we'd just totally turned the field on its ear, ten years. To list the things that went on in those ten years, I'll start with the things that I cared about the most.

GC: Okay.

EF: First was Dr. Zubrod said that we should work on leukemia. So the problem was where do patients with leukemia come from? So we have to talk to the doctors. Well, the doctors said, you know, "To send a patient of mine to a bunch of young guys who don't know anything, who are going to experiment on my patient is ridiculous." No one wants to do that.

It wasn't easy to get patients out there in the country in Bethesda. "Besides, who wants to drive 35 miles every day to take care of my kids?"

So we had to recruit patients. So what we did is we systematically began to visit medical societies, hospitals, clinics, patient advocate groups, and we advertised what we were doing, "Here's the research we're doing," trying to impress them with our compassion, "We don't experiment, we give them treatment, we're making progress." We began to build a practice. And that was item number one, we had to build a practice. We had to be good, we had to have good relations with parents, with the children, and universities.

In that regard, one of the experiences I had will interest you because we used to have our annual meeting of clinical research societies in Atlantic City. And at one of those, the President of the Society was the Dean at Hopkins Medical School in Baltimore. And he gave a speech that actually condemned the NIH. He said that research cannot be separated from practice and education. This is the Oslerian model of the three legs of the stool. That is, you can't discover anything about disease if you don't engage in teaching, in practice, service work. At the Clinical Center we only did research, no service work. The only patients we cared for were patients that we accepted for our research. And there were no students, except for Fellows, and they basically were like graduate students; they weren't undergraduates.

But despite that, our practice grew because we did a good job. We took good care of them, were good to the family, and we had extraordinary resources, and it was <u>free</u>, and still is free.

GC: Very important.

EF: So that the money they spent travelling, they didn't consume in their medical expenses. And you see, that's a principle we have to get back to.

The way we're going now as a country—I'm going to mix this up with what's going on now and what happened then, because if you compare what happened then to real progress in ten years, to what's happening now—you see, now research is funded out of this managed-care business. It's out of our medical practice. It's all fee-for-service. We have to get back to the notion that things that are really original, for people who are willing to participate, it's got to be free. The community has got to support research. They don't do that anymore—only at the Clinical Center, not at M.D. Anderson. Here everybody has to pay for their care.

So we built our practice, and we devised some very simple hypotheses based on Law and Goldin's animal experiments. That is, we began first to investigate combinations of drugs. That was our first protocol. Frei probably told you about that.

GC: Yes.

EF: Then we decided that although our practice was building, if you did the arithmetic, we didn't have enough patients to really get definitive answers in the control trial. We needed more patients. So we formed the first cooperative group. We called Jim Holland, who had been there I think for a year or two, and said, "How about the Roswell Park and NCI cooperating?" because Roswell Park was like us. It wasn't a teaching or a service institution, it was for a research institution.

So we had a cooperative group. We called it Leukemia Group. And we devised a protocol, and we both used the same protocol. And we did a study and we published it. And then we moved on to a little more complicated study where we were looking at schedule of administration.

But the advantage of these early studies was that we began to define quantitatively the natural history of childhood leukemia. We began to know what the likelihood is that you'd respond, what the duration of response was. We worked out the variables which predicted for response, and the variables which we could use to predict recurrent disease.

So we were moving along, and one day Gordon Zubrod, to his credit—he never totally lost contact with the people doing the work, so he used to come on rounds every once in a while. He came on rounds one day, we were walking through the ward, and we came into a room where there was a child who was about four years old who was dying of his leukemia. He'd been treated, and he was refractory, and we didn't know what to do for him.

And in the terminal stages, they develop a hemorrhagic diathesis. So this baby was lying in his bed, semi-conscious—he had meningeal leukemia, we know now, and he was breathing kind of irregularly because he wasn't—just like you would if you were snoring or something like that. But he was bleeding from his nose and mouth everywhere. And when we walked into his room, the whole room was covered with blood. The nurses were scrubbing the blood off the walls and changing the sheets.

Zubrod said, "Freireich, why don't you do something about this bleeding?" "Yes, sir!" So I actually did. I went back to my—I didn't know anything about bleeding—I went back to my lab and I began to work on this problem. And what I did was what a surgeon would do, you know. I said, well, let's see why they're bleeding. So I looked at the blood, and I said the major change is they don't have any platelets. Everything else is okay. So what if I took the blood from a leukemic child and I took platelets from my blood, and I mixed the platelets in their blood, would it behave normally? And sure enough it did.

It wasn't a terribly original experiment. A lot of people had published that before. And then I began to inquire about how you would go about replacing what platelets had. So I had a friend, Ed Korn, who is now the Scientific Director of the Heart Institute, who lived across the street, and he was working on lipids. Heparin-associated lipids. That's the other nice thing about NIH is, see, they're all right there.

And they were doing—the ultracentrifuge had just been invented, and they were separating lipids like they do now on more sophisticated equipment. I said, "You know, we know that the parts of the platelet that can accelerate the coagulation process, so-called procoagulant—are all lipids. I wonder if I gave you a preparation of platelets, if we could separate all these lipids and see if I can identify the procoagulant." So he did that. And we sonicated them in a machine—I got that machine—and put them on an ultracentrifuge, and we cut the tube—we used to have a tube-cutter, I actually did it mechanically—a plastic tube, and then we took these layers out and threw them back in leukemic children's blood, and we found out there was a thing, and it turns out this is now called platelet factor 3. And so I said, well, let's get platelets from normal volunteers and make a whole tube full of this platelet factor 3, and see if we can inject it into children and stop their bleeding. And so we did that. And, by golly, it worked like magic!

Children were bleeding to death, and I'd take a bag of this lipid that came out of platelets and shoot it into their veins, and they'd stop bleeding immediately. We measured it quantitatively, and I was very impressed. I said, "Now we've got something."

There was only one problem. The problem was that as soon as you stopped infusing the lipid, the bleeding came back. And by studying the blood, we could tell what was happening. That is, these lipoproteins which circulate for a very short time—their half-life was an hour—so unless you were constantly shooting them in, they were removed and you're back to normal.

So we said, "By golly, that's what the platelets do. The platelets are a packet of procoagulant that circulates in the blood, and when you injure the vessel, it sticks to the vessel"—this had all been worked out in animals—"and it discharges the procoagulant locally. So basically, a platelet is like a liposome. It's a carrier for these procoagulant lipids. So obviously, why am I wasting my time doing all this? I've destroyed the platelets to make the thing that clots, and they don't have a carrier. Why don't I give them platelets?"

So we said, "Hey, that's a great idea." So we did a couple of pilot studies with—we didn't know how to separate platelets at the time, but we decided that we would study the lifespan of platelets in banked blood.

So in the laboratory I looked at how long platelets were intact as an organelle in a store of banked blood. And we found out that over the first 48 hours, in the cold or at room temperature, the platelets would disintegrate. They had a very short lifespan in a bag. So we said, "That's why blood doesn't work, because the platelets are all dead. So we have to give them blood that's drawn immediately, fresh." And we did—I still have the graph, I never published it—we did a child—because Gordon Zubrod stood at my side and we did this—his name was Scotty Dinsmore, and I knew the family very well, and I loved this child. And he was dying from hemorrhage.

He [the father] worked for the CIA or something and he could get a hundred people, and we said, "Here's what we're going to do. We're going to exchange-transfuse this child. We're going to take his blood out and put normal blood in and see if we get his platelet count to normal." We actually did that, one syringe at a time, 100 cc's, a little four-year-old child, all those donors. We spent about six hours doing that, but it was true. We got his platelet count to normal, the bleeding was totally controlled. The platelet lifespan we worked out was about 30 hours. They all disappeared, so that in three days he was bleeding again. But that's a lot better than 30 minutes.

GC: Right.

EF: So I said, "We've got to get platelets again." So we got these people back in—another 30 hours. Well, you can see that we've got the idea. Now we have to figure out how to do it.

So the first challenge we faced—Dr. Zubrod and Dr. Frei may have told you this anecdote about the platelets. Did they?

GC: Well, tell me. I don't know yet.

EF: It was an amazing event. So the first thing we had to do was we had to convince the blood bank to give us fresh blood, and we did that. And every time we gave them fresh blood, the bleeding stopped. So we said, "This is the treatment." "No, you can't be sure because it doesn't always work, and the times it doesn't"—so on and so forth—"you have to do a controlled trial."

What is a controlled trial? A controlled trial is a form of human experimentation. That is, you're going to give people the treatment you know doesn't work and randomly allocate them to a treatment that you contend does work.

This is a mentality that we started, that is tragically now the most important impediment to clinical research. [Laughter] But at the time, we didn't have any other way to go. Because remember, if you're going to give people fresh blood, it's very expensive, time-consuming, a whole change in the routine for blood-bank directors. Blood-bank directors don't like to change their routine, you see. They're not investigators.

So we had a negotiation with the blood bank. We had a very emotional confrontation with them. They said, "This is ridiculous. You cannot do it. It's all silly. It doesn't work. Freireich's lying. He's a cheater. He's a crook. He rapes children,"—whatever.

GC: Oh, my gosh!

EF: No, I'm just exaggerating. The point is—"this can't be done." So we negotiated over a month or so, and to Zubrod's credit, the way it went was this: The forces of evil called in all the experts in the world, and we had a grand rounds on the top floor of the Clinical Center in the auditorium. And they presented the evidence that fresh blood would not work. And then Frei and Freireich crawled in at the very end and said, "Well, we have 20 children and we gave them these things and it seems to work." And then the conclusion was, by the great Professor Brecher, who was then running the show, and Paul Schmidt, "we have demonstrated unequivocally that these doctors who ordered fresh blood, they're spending money unnecessarily, experimenting on children, and they're stupid." So that's the end of grand rounds. So Dr. Zubrod put his hand up.

And he said—I don't have the exact language. He would probably remember it, or Tom [Frei] may remember it. But he said something to the effect that "Our job here is to discover new approaches to the treatment of disease, and I'm director of the Clinical Center, the National Cancer Institute Clinical Program, and if the doctors on my staff order fresh blood, then you'd better deliver it."

And he sat down, I remember it—[laughter]. How do you like that? He stood up and supported the young guys—to his credit. He didn't know whether they were right or wrong.

I'll tell you another anecdote in a minute about Zubrod. Do you like anecdotes or are they boring?

GC: No, I think they're what makes history.

EF: Okay, that's what makes history. So after that, we sat down—it was obvious that they weren't going to put Zubrod down. So they only had two choices. One was to cooperate with us and provide fresh blood, which they didn't want to do, or else set up some plan where we all agreed that the answer would be no. And they were sure that we were wrong.

So we agreed to do a randomized prospective controlled trial where the blood would begin as fresh blood drawn within the last 48 hours, or blood which had been in the blood banks for more than 48 hours, usually up to 21 days. This had low or no platelets; this had good platelets.

And the way it was done is when a child was bleeding, I would measure the amount of blood in the urine quantitatively, from his mouth, petechiae—I would count them. We actually had a machine where we did petechial counting and bleeding times and all this objective stuff, and then we gave them their blood by replacement. And they were assigned by a statistician either to receive fresh blood or banked blood.

We did this for two or three months—we didn't have all the formal stopping rules we have today, but we decided after we had 20 or so patients that it was time to look, because we knew that some of the children had stopped bleeding and some had not. So if there was heterogeneity in outcome, and there was heterogeneity in treatment, it was possible that there was a result.

So how are we to break the code? The way we did it was the statistician, the blood bank guys—the bad guys—and the clinicians—Tom Frei and I, the good guys—sat in the same room and it went as follows.

Patient Number One. Freireich says Patient Number One stopped bleeding, and here's the data—bleeding time, clotting time, and so on, after transfusion.

Patient Number Two. Freireich says no effect, bleeding continued, nothing happened.

We did that for all the patients. And then I sat down and the blood bank director got up and said, okay, here's what they got, Patient Number One got this, Patient Number—

We didn't need a statistician; it was day or night.

GC: Really.

EF: So everybody looked at everybody. What do we do now?

[Laughter]

EF: The next thing that happened was the blood bank director wrote a memo to the Scientific Director at the Cancer Institute that said that "Freireich cheated," because—and this is the actual memo—"What he did was when a child was bleeding, he sent the parents down to donate blood that was required. And then the parents came back to the ward and Freireich asked them whether they gave their fresh blood or didn't. And therefore, he knew who got fresh blood and who didn't, and he Mickey-Moused this whole show and it was all a pack of lies, and I refuse to participate in it."

So our Scientific Director then, G. Burroughs Mider, was a pathologist who was terrified of being criticized by anyone—typical bureaucrat, you know. Bureaucrats can't do anything that might expose them to risk. That is, if they make a mistake, they get fired. On the other hand, if they discover the cure for cancer, no one will know it because they're just bureaucrats. So they're all very conservative.

So Dr. Mider got this letter, and he called me to his office. I'll never forget this confrontation because I just couldn't believe it. I mean, he called me to his office—a young, idealistic, ghetto-dweller, here trying to cure leukemia, working 20 hours a day, got kids at home and no money—and he said, "You're a liar and a cheat, and if you don't stop this lying and cheating, you're going to be fired."

GC: That directly?

EF: Directly. There was no question about who was right or wrong.

So I went back to the forces of good. I spoke to Tom Frei and Gordon Zubrod, and "Mider may be right, maybe I was a liar and a cheat. How do they know?" You know, I might be a liar and a cheat. But these are people of quality. So they said, "Well, I don't see any evidence of lying and cheating. We participated in this fully. We're going to publish it."

The blood bank director took his name off the paper. The guy who ran Lab Medicine, the other end of me, Brecher, agreed to put his name on the paper, and we published the first prospective randomized trial that proved that fresh blood was better than banked blood.

I have to tell you that we had one other objective piece of evidence, and that is we did platelet counts on these children, and we were able to show that the difference in platelet count between those that got fresh blood and bank blood was 5,000 platelets per microliter. It's important for you to understand the normal platelet count is 200,000. This is 2.5 percent of a normal value. So it's difficult to measure.

But the method had been invented by George Brecher, then at the Clinical Center, which was phase microscopy counting of platelets. And I did these counts in my own laboratory, sitting there with a phase microscope counting the little particles.

So here we are again, we had other objective evidence, but remember, it was Freireich who's a liar and a cheat who says that these counts were correct. So you had to have faith in whatever he said was right, but we published this paper. It appeared in the *New England Journal of Medicine*. It got a lot of critical reviews published.

Okay, so this breach has never been healed, by the way.

GC: Really.

EF: Yes. [Laughter] These people are still mortal enemies. Mider is dead, but . . .

What we did next was we said, "If one unit of fresh blood can give you an increment of 5,000 per microliter and stop the bleeding in 70 percent of children for 48 hours, what if we gave them two units?" "Well, how would you go about getting two units? A child—you can't give him two units of blood because his blood volume is too small to absorb all that.

So I went to literature and I read. E. J. Cohn invented a machine for plasma separation, and my old professor, Armstrong, had worked on plasma separation. He says, "Well, look. What if we took the unit of blood and separated the plasma from the red cells? We could give two units of plasma, rich in platelets, and only one unit of red cells."

Guess what happened? The increment for two units of plasma was actually 12,000 per microliter on average, and the effectiveness was about twice as good. It lasted twice as long, and twice as many people responded. "We've got something here. How do we systematically get to use blood?"

Well, I sat down with a young clinical associate named Alan Kliman and Fenwal had just marketed plastic equipment for collecting bags instead of glass bottles and rubber tubes. Plastic was just coming in. And the nice thing about plastic, it's flexible, it can't break, you can store lots of bags instead of all these bottles. So he said, "Maybe we can use this plastic."

So we sat down with a bunch of tubes and things and we put together a thing—I can give you reprints of all this. It's all published. It's really interesting. And we made a two-unit closed-bag system, which was used for 15 years. And the way it works, is you stick a needle in the donor, you take a unit of blood, you have an I.V. to keep the needle open, you take this thing out, stick it in a centrifuge, take off the platelet-rich plasma, hang up the blood, put the red cells back in. Bleed a second unit of blood into the second bag, repeat the procedure. You've got two units of platelets, all closed, sterile, and you've got two units of platelet-rich plasma.

So then we began to study two units of platelet-rich plasma systematically in treating hemorrhage. And the way we did it was we got 12,000 per microliter, so if you gave a child two units of blood, we'd have 25,000 platelets per microliter increments. The half-life of platelets was about a day and a half, two days, so we could we could transfuse a child every three days and keep his platelet count out of the bleeding range.

I had a Fellow in my lab, Larry Gaydos, who did a paper, which is a citation classic in the world's literature. It wasn't original, but no one would ever take the time to do it. We sat down and analyzed all the hemorrhages in all the children and correlated the platelet count with the bleeding. And we knew that the threshold for bleeding was about 10,000 per microliter. And if you're above 20,000, the frequency of major hemorrhage was very low, so we did systematically two-unit plasmapheresis treatments every three days in children, and by the time we did for four or five years, Drs. Hersh and Bodey, who are both big professors and are still here, wrote a paper in which they analyzed at autopsy the causes of death. And what happened was that with the two-unit bag of plasmapheresis, where hemorrhage was the leading cause of death prior to platelet transfusion, in a period of ten years infection became the leading cause of death and hemorrhage almost disappeared.

And this is the treatment that is universally used around the world in 1997. That was 1957.

Of course, a lot has happened since then, and we did a lot of it in that ten-year period. We really went at it. Because what we did was, the first question we asked was, "How much can a donor donate?" So we got some volunteers from Pennsylvania that lived in the Clinical Center. They were unemployed people, and they got food and board and their $25 a day, and we bled them until their platelet counts and the albumin went down, and we published the limits on platelet donation. And the Red Cross and the ABB use it today, one liter per week is the limit you can give. After that, you begin to deplete the donors. So that meant that a donor could give four units of platelets a week.

And then people invented four-unit bags so you could take four units at one setting, so a donor would give once a week. It gives four units of platelets. You can maintain a child with two transfusions a week, one donor/one recipient—terrific.

And then we'll get into the machines, because I invented the continuous-flow blood-cell separator, the same thing. We needed a way to do this automatically. Now it's all done by machine. So we have single-donor platelets. The donor comes in, you get four units of platelets. The machine spins off the platelets, returns the plasma and the red cells. You get 4×10^{11} platelets in a single donation—terrific. So the platelet transfusion thing was solved.

Then we had other problems we had to worry about. We had to worry about storage, how long could they be stored? We did experiments on how fast they disappear, and it's all being done today. We did experiments here in which we showed that you move the platelets. There's a lot of technical improvements, but the basic breakthrough occurred very early, and it all came out of Zubrod saying, "Why don't you do something about bleeding?"

And shortly after we implemented this, after Zubrod had made his dramatic appeal and we had got the thing working, he came on rounds again. And we had a rule on rounds: If anyone ever saw a drop of blood in the room, then the doctor was immediately reprimanded because we knew how to control it. And there was no blood on the walls, no blood on the bed sheets. And that's true today. If you go on a leukemia ward, you won't see anybody bleeding.

Occasionally patients become isosensitized. We still have a few problems with bleeding. We haven't solved the long-term storage problem. And technically, it's going on and on. We learned how to make concentrates and a lot of technique stuff. That was a very important breakthrough.

The second important breakthrough—

[End Side B, Tape 1]

[Begin Side A, Tape 2]

EF: So the next thing that happened was we reasoned—the chemotherapy we'll come back to in a moment because these things are going on in parallel because we were committed to curing leukemia, so we had to do everything that was necessary. We realized that if children died of hemorrhage, we didn't have time to cure them.

So we had to take care of their hemorrhage. We realized then that they were dying of infection. We had to get rid of the infection. Well we had antibiotics. We began to do—Jerry Bodey became the world's authority on the antibiotic therapy of children, and we introduced some very important concepts into infectious disease. We were the first group in the world to use antibiotics empirically. What that means is when children or adults developed a fever, the normal practice is to identify the cause of the infection before you choose the antibiotics.

But we recognized that for these children who were dying of infection, that the commonest cause of infection—we're now in 1957, '58, it's not true today, so don't get it out of context—was *Pseudomonas aeruginosa* because we didn't have a good antibiotic for pseudomonas. The antibiotic we had was polymyxin and it was only marginally effective, and if we waited, the time to a positive blood culture identification was about forty-eight hours and if you had pseudomonas infection, the mortality from that infection in a leukemia child undergoing therapy was 50 percent.

So you had a 50 percent of dying—chance of dying of infection which was the leading cause of death in the 48 hours required to make the diagnosis. So we said, "Obviously when a child gets fever, we draw the cultures. But we're not going to wait for the results, we're going to start polymyxin." And we were able to show that that works dramatically because the difference between treating at time zero and time 48 hours is life and death. There's got much more infection and that antibiotic doesn't work where it will work early.

So we introduced empirical therapy, we used broad spectrum antibiotics, we introduced several new antibiotics, Dr. Bodey as I say is the world's authority, all started when we were at the Clinical Center. So that was another major breakthrough.

Okay. So now we were left with a circumstance where despite the empirical antibiotics we were giving, and despite the platelet transfusions, the mortality that was occurring was still dominantly due to infection with organisms that were resistant to the antibiotics we had. So what are we going to do about that? Well we did the same thing we did with platelets.

We said, "Go back to the lab and ask yourself, 'Why are they getting these infections? These are organisms that wouldn't kill you and me, they're killing these children. Why?'." It turns out they don't have any neutrophils. So Dr. Bodey, who's still here, did a study comparing the neutrophil concentration to the risk of infection, and it turned out like platelets. The fewer neutrophils you had, the higher the likelihood of infection.

What's the solution to that? What if we gave neutrophils from normal people to children with leukemia? So we said, "Let's do it." So we went to our four bags for platelets and we started to transfuse granulocytes from normal donors. Now we knew the limited donation was four units a week, so we did that, and after we did about ten children we figured out nothing was happening. Totally useless. Why? Well, we went to the literature and looked up the physiology and it turns out—I have to give you some quantities, do you mind that?

GC: No, that's fine.

EF: Okay. In your circulating blood, the number of neutrophils you've got is about 10^{11}. That's 1 with 11 zeros. Lots of neutrophils, but they're very small. It takes a billion, 10^{9}, for your tip of your finger. So 10^{11} is only 100 grams, about that much buffy coat. When we did 4 units of blood, the number of neutrophils we had was only 10^{9}, 1 percent of what we needed. So the consequence was when we dumped those few neutrophils in the blood, nothing happened.

So Alan Kliman, the guy who worked with me on this thing at the blood bank—he had a family and we had a family—we were at a cookout in his backyard one day and we were talking about this problem and he said, "You know, you've got to do something about this neutrophil thing." So we came up with a brilliant idea. What if we used granulocytes from patients who had chronic leukemia where they have granulocyte concentrations in the blood that are 100 to 200 times higher than normal people? They're sick, but what we if took their neutrophils and gave them to the other leukemia children?

Oh my God, if you tried to do that in 1997, they'd lock you up like you were insane, you know, there's no Gordon Zubrod defending us any more. But in that day, in that age, Zubrod said, "Sounds crazy. Let's do it."

So we started to do the two-bag pheresis from donors who had CML and we collected 10^{11} granulocytes and we shot them into children. We did 100 transfusions. We wrote the first paper showing that granulocyte transfusions could be effective. No doubt about it. It was just like the platelets.

If you could get the granulocytes from a normal donor, and elevate the granulocyte count, you could control infection. Now how should we do that? I just wrote a little thing—I'll give you a copy of it—I just wrote a little history of this. Because what followed was we said, "We've got to get granulocytes from normal donors because if you take them from CML donors, there aren't enough patients around to take care of neutrophil. We've got to figure out a way to get granulocytes from normal people because we want healthy granulocytes, we've got to get 10^{11}, how are we going to do that?"

So we did a little thinking like we did for the chemotherapy. "We have to collect all the granulocytes that you have in your blood! Five quarts! How are we going to do that?" Well, I said, "One of the things we can do is work out a collection system, a centrifuge, that would skim the granulocytes out of your blood and we could run the blood through it like an artificial kidney. Continuously, continuously, continuously, until we got all the ones we needed."

What about that? Great idea. There was a blood cell separator on the market, the Cohen machine, which was a batch flow separator. It's still commercially available. What it does is it takes a unit of blood like we did the platelets, separates the buffy coat, puts it back, does it again, over and over again. I said, "We'll never get there that way."

I mean, if you do the arithmetic, even if we collected 100 percent of the granulocytes went through the machine, you can't take your whole blood volume out and spin it. We can only take a little bit at a time, so if you take a little bit at a time, you have a dilution effect. As you deplete it, you're getting less and less. So if you do the arithmetic you have to process the blood volume at least twice, so if you can do it by batches, this would take three days, and no way.

So I have to have a continuous flow machine. So I started to work in the laboratory on a way to get blood separated in a centrifuge so that the blood continuously separated. I started with electrophoresis and then I worked with membranes which some people worked with and worked, and I remember Tom Frei used to come into my lab, I tried to use mechanical flow.

It turns out that in capillaries, the granulocytes tend to flow along the edge and the red cells through the middle. There's a laminar type of flow, so I figured if the path was long enough it would work. But as the path gets longer, the pressures you need to move it were higher so I used to have these tubes running around my lab all over the place and shooting things and doing mice.

Well anyway, we were doing this and one day a guy appeared in my office, his name was George Judson. His son had developed chronic granulocytic leukemia and Dr. Block, who became the director of the Clinical Center in later years had seen him, and he said, "I'm an engineer, is there anything I can do?" He said, "There's this crazy guy on the twelfth floor who's trying to separate blood. Why don't you go see him?"

He appeared in my office and he said, "I want to do something. You want to separate blood." I said, "Yeah." So I sat down—and I wrote this in the story—and I said, "Here's what I want to do. There are seven things I want this machine to do." So he looked at that, he didn't know much about it. He said, "Okay, let me go away and think about it." He went away.

I'm running my tubes and things and he came back about a month later, and he said, "Here's my plan." Sounds pretty good. How are we going to do this? He worked for IBM, he went to his boss, IBM was very interested in employees. He said IBM gave him a kind of a sabbatical. They paid his salary and let him be stationed in my lab. I had to write a letter saying I'll be responsible for him, Zubrod had to approve it.

And sure enough he began to commute from Endicott, New York, to Bethesda and building this machine. He would pirate junk parts out of the IBM factories there where they were making computers and borrow from the brains of engineers and he put together a Mickey Mouse deal—we have a picture of it in my lab—and we ran blood that we got from the blood bank which was outdated or not used, and we worked hard and we thought we had it working.

So we went to Zubrod and we said, "We want to do this on a patient." "Are you crazy? You have to work on horses, cows, sheep, mice, dogs, elephants." "No, we don't want to do that because all those animals have different blood, different set of sedimentation characteristics, we've been working with human blood in vitro, we want to go directly to man." "You can't do that." But anyhow to his credit and Frei's credit, they allowed me to do it.

We took this Mickey Mouse clap trap thing and we collected white cells from a patient with chronic granulocytic leukemia who were being donors for our granulocytes. We showed it would work. But everything was clap trap, you know. The pumps didn't work very well, the seals were leaking. So the idea was correct, but we didn't have the equipment.

So we convinced Zubrod to convince the advisory committee to give us some money and we issued a contract to IBM. They went to work and came up with a machine, the first continuous flow blood cell separator in the world. It's actually patented, and Mr. Judson and I jointly hold the patent. So it's in the public domain.

IBM has subsequently pulled out of the business and it's now marketed by COBE [Laboratories] as "the" blood cell separator in the world. It operates exactly according to the seven things that I wrote.

I actually have the paper that I wrote down with Mr. Judson, and we accomplished exactly what I set down as our task and it's commercially available and dominates the world today. The important thing about that is when I came here, we continued this collaboration with IBM and we continued to separate blood cells. As you know, Steve Rosenberg's world famous for LAK cells. He'd never been able to do that without the blood cell separator. We were the first to show that stem cells circulate in the peripheral blood. Using our blood cell separator here, now the world does bone marrow transplant using the blood cell separator for peripheral blood stem cells. We were the first to show that you can collect granulocytes and now, with growth factors for mobilizing cells, we can make a normal donor like a CML donor. We can put his counts up to a hundred thousand and then we can get enough granulocytes from a normal donor.

We invented the hydroxy ethyl starch and etiocholanalone. All that went on at the Clinical Center in that ten-year period. We got the bleeding problem controlled, we learned how to separate blood cells, we invented the continuous flow blood cell separator. And that's all trivial, that's all background. That's supportive therapy. The important thing we did was we cured leukemia.

Now, how did we cure leukemia? Well, I had a very good friend who was an intern, a resident with me at Presbyterian Hospital with S. Howard Armstrong. His name was M. C. Li. Have you heard the name?

GC: Yes.

EF: Dr. Li was Chinese, his father was Christian Evangelist. Communist Revolution occurred, he was an outcast. Father and wife in prison, he came here for a fellowship; he couldn't go back. So U.S. gave him compassionate citizenship or whatever they call it. After I went to Boston, he went to New York at Sloan-Kettering and worked with Olie Pearson, and as fate would have it he ended up at the Clinical Center, very shortly after I got there.

M. C. and I had dinner together, and actually about a year after he got there, the Communist revolution thing quieted down a little bit but he wouldn't go back. He was already successful so they let his wife come out. She came over, and the first day she was back, in his apartment, she cooked a Chinese dinner for my wife and I and M. C. and his wife. It was quite an occasion. She couldn't speak a word of English, but she was a lovely lady. She eventually became rich and Americanized like all people do.

But M. C. was even more radical than me. M. C. was the first person—you know it's amazing what he accomplished. First of all, he had when he was working at Memorial made the observation that methotrexate inhibited the chorionic cells in mice. And he made the giant leap, an intellectual leap, to the fact that in man, there is a tumor of the placenta called choriocarcinoma and he said, "Maybe methotrexate could involute this like it does the placenta itself."

Methotrexate was the leading abortifacient in the United States for the last fifty years. If you take methotrexate, it kills the placenta. And since this is a tumor deriving from chorionic cells, he said, "Maybe this would work." Now, because his training was endocrinology, he also knew that the chorion, the placenta, produces a hormone that is necessary to sustain the growth of the placenta. That's chorionic gonadotropin that's made by other cells in the body but uniquely by the placenta.

So he began to study these women with choriocarcinoma and he discovered that they all had enormously high levels of chorionic gonadotropin. So he said, "This must be product of the tumor." Do you understand? The first tumor marker. Tumor marker is now a big field in cancer. But he conceived of this hormone being a marker of how much cancer they had, and he showed that the ones who have lots of chorionic gonadotropin have the shortest life span, the ones who have less have a lesser life span. This was important.

Now he figured out methotrexate. He went and talked to the pharmacologist, Paul Condit, who was working on methotrexate doses and so on, and he got the idea that if he gave these women not the conventional dose of methotrexate but a very high dose of methotrexate—he was the first person to do high-dose methotrexate—twenty-five milligrams of methotrexate a day for five days, what would happen to the chorionic gonadotropin.

He treated the first lady, Mrs. Boxer, and she has been written up in every magazine in the world. The first patient he ever treated is still alive and has had children. She was dead when he treated her. Literally dead. Bleeding from every orifice, cancer all over the body. Shot her with methotrexate. She had a miraculous response. Turns out now, in the perspective of 45 years later, if you did it that way in all women with choriocarcinoma, that stage of the disease, you'd only cure one in four or maybe one in five. But she was one of the lucky ones. Had a terrific response.

But Dr. Li was not satisfied with the clinical observation. He followed the marker and what happened was, when her disease went away entirely and she was completely normal, ready to go home, he looked at chorionic gonadotropin in the urine and it was still elevated. Ten times normal. He said, "I think this lady has cancer. She needs more treatment." He was the first one to do that. To treat people without disease, based on a marker.

And he showed that when the chorionic gonadotropins get to the normal level, nobody's cancer comes back. If you stop treating and they still have a level of chorionic gonadotropin, they all come back. So he discovered the first tumor marker. He cured the first systemic human cancer. Fantastic breakthrough. That all went on right under my eyes. We talked to him every day, saw those ladies in the clinic. Of course Dr. Li was fired because he was too radical. The one who gets the credit for this is Roy Hertz. Do you know Roy Hertz?

GC: He's on my list, too.

EF:M. C. Li was the mover. But he was Chinese and he was easily victimized and they fired him. And subsequently Hertz and Bergenstal and Lipsett got most of the credit for the cure of choriocarcinoma. But see this went on under my eyes, but see, that was a great breakthrough for those two reasons: you treat people based on a tumor marker and you understood that you could eradicate a cancer that was systemic.

But choriocarcinoma is not like other cancers. It's a cancer of the fetus, so it's an allograft. So everybody said that's great to know, because women all died of choriocarcinoma, but the fact of the matter is you weren't curing a cancer where the cells did not come from the person. These were cells from the fetus. They were half paternal cells, so they're not a syngeneic tumor.

"No one can ever cure a cancer . . ." so that's what we did. We made the leap from choriocarcinoma, an allograft, to curing childhood leukemia. And we were the first people in the world to claim that a systemic cancer could be cured with a chemical. Because up to that point, everybody was convinced that if surgery and radiation didn't control the local disease, that once it was systemic it was hopeless.

Well, we claimed that ALL, acute lymphoblastic leukemia, in children could be cured, and we were right. And in the context of forty-four years, we proved we were right. And the way we made that prediction was based on kinetics that Dr. Frei and us and Zubrod derived from the animal model that was studied by Skipper and Schabel.

I don't know if you're going to interview Skipper, Frank Schabel's now dead, but Howard Skipper's still alive. They worked out the kinetics of leukemia, a transplanted leukemia in the mouse, the Lloyd Law L 1210, and they showed that you could measure the amount of residual cells, because you can't count all the cells, but they showed you could estimate it from the time it took for the cancer to come back.

So if you were making progress toward cure, then the interval without treatment should be prolonged. We conducted the first—and it's a citation classic—with Ed Gehan. Are you going to interview Ed Gehan?

GC: He's another name I have, yes.

EF: He's at Georgetown now. He was the statistician on the first randomized prospective placebo study where we did adjuvant chemotherapy, that is we took children who were in complete remission and we said, "Would it matter if you gave them in complete remission treatment even though they have no disease? Or not?" And we showed clearly that the children who didn't get treatment, the leukemia came back in a median of eight weeks, children who got 6-MP, the disease came back in a median of thirty-three weeks, what we began to see something funny.

There were a few stragglers out here. Was that significant? Just a hint. An occasional patient went longer. So, I said, "Wait a minute. Maybe something's going on here. Maybe we can eliminate childhood leukemia."

So what we did was we measured the time to recurrence in the children who had first remissions was X, the children who got the adjuvant chemotherapy it was significantly longer. So we just did a little bit of arithmetic, and we said, "Look. The problem is we only treated these children for three months. We've got to treat them longer."

So we started studies of intermittent reinduction, we treated children for a year, and while we were doing all this, we were also doing the combination studies.

The big breakthrough occurred when—this is going to be a difficult story to record and maybe it's, you've got to realize it's a one-side view, it's my side—but what happened was we were very anxious to develop new drugs, and we tested a number of compounds that were active in mouse tumors that came out of the screen. Dr. Zubrod initiated the screening program of the NCI. We had the opportunity to study some drugs. I went to a meeting and I heard Irving Johnson present a study of a drug called vincristine, the vinca alkaloids, and they gave vincristine to patients, [Eli] Lilly had a clinic and they gave it to patients with cancer because leukemia was a rare disease, they didn't have any with leukemia.

So the amazing thing to me about vincristine was that the tumors could regress but it was not suppressive to the bone marrow. So I said, "Leukemia is a disease of the bone marrow. If we had a chemical that's not suppressive to the normal cells but would kill the leukemic cells, this is what we've been looking for." So I called Irv Johnson and we talked and he said, "Clinical trial . . . we'd like to get it into a bigger clinical trial."

So he came down and we talked, and went to Zubrod and Zubrod said, "You know, Freireich, we are trying to develop a systematic screening program. We're using L 1210. Vincristine is a drug that does not work in L 1210 and we know therefore it won't work in childhood leukemia. So you are wasting your time."

This was another Zubrod greatness. I said, "Dr. Zubrod, I have all the faith in the world in the L 1210 screen but I am very impressed with vincristine. I want to study it with children." He said, "What you have to do, Freireich, is you have to go back and work with Goldin and Law, and get the L 1210."

I said, "I don't want to do that. I'm satisfied that Dr. Johnson has responses in P-3-88 and I want to go directly to children. I've got a ward full of kids who are dying. Benefit, risk, they ought to do it." So to his credit, he said "It's wrong, but if you want to do it, you can do it." Very careful. One child at a time.

Well the first child we treated had the most dramatic response of anyone. It's like I told you about research. Early success has a big impact. The first twenty children we treated were reported by Myron Karon. We had something like six complete remissions with a single new agent. It was just night and day, and the hypothesis was correct. It was not myelosuppressive. So Frei told you the story about—did you talk to Frei?

GC: Yes.

EF: He told you the story of how we thought of nonoverlapping toxicity. You know, when he and I talk about things, we have different perspectives, but we were one mind. We saw each other twenty hours every day. I mean, we didn't even do things socially without being together so we were really one people thinking. The basic strategy was we had known about 6-MP and methotrexate, we knew about prednisone and 6-MP, we knew about prednisone and 6-MP and methotrexate, and when vincristine came along I went to Frei and I said, "We've got to do it. We've got to give vincristine and prednisone 6-MP and methotrexate."

"Ridiculous. You can't do that. It's a new drug. We don't know. It's impossible." And Zubrod said you can . . . But you know, after a lot of haranguing, they said, "Well, we just have to do it."

And we did it. We treated twelve children. Eleven of them went in remission. It was so dramatic, it was like falling off the chair. We called it VAMP. We invented the first, whatever you call these things, you know, the initials, the acronym for a chemotherapy. It was VAMP. It's very famous now.

It was so dramatic that we began to think about choriocarcinoma. "Wow. If these children sail into remission with no toxicity, one course, two weeks, this is really exciting. What if we continued it in remission? Could we get to zero?" So we did our arithmetic, and we said, "Look. If the time to recurrence is . . . . What if we gave them three treatments when they were in remission?"

Now can you imagine the impact of this on that service? We used to have a meeting with these parents and the children. You know, life's greatest tragedy is to lose a child. I mean you can lose a friend, a relative, mother, father, but children. It just inverts your whole life because children are full of life and you're old. It's difficult for these parents, decisions.

So we went to them and we said, "Look. I've got your child in remission. What I want to do now is put them in the hospital and give them a treatment that might kill them, but I think it is a chance to cure them. If we don't do something, their disease is going to come back because we know they all die."

Remember we had this little thing over here. Just maybe there are a couple of people who really were being cured. And these parents went with us and the kids went with us and we did it. We treated these twelve children in remission. We put them in the hospital, it was a very emotional time. We did our calculations, you know, who's going to relapse and . . . . They didn't occur all at one time, they occurred over a period of time. And then all these parents were there and we were all waiting. Were they cured? Or weren't they cured?

One child relapsed. Oh, God, look what this means for us. Then a second one relapsed, a third one relapsed. Of the first twenty-seven, there were maybe six or seven who were cured. So we were beginning to get discouraged by the time we got to twenty-one. But there is no doubt that by the time we got, we got to the point where the calculations we had made based on the doubling time of the cells and based on how long it took for them to be diagnosed, that we were certain these children were cured. Because otherwise, their disease should come back.

So we had five or six of them still in remission. We wrote this paper. We said, "We think we cured leukemia." And of course it was true. What we did after that was to go on to, we did the first adjuvant therapy which is now widely practiced in cancer, we did the first early intensification which is now routinely practiced.

Then we went on to what we call the POMP, intermittent re-induction which is now universally practiced. And now with ALL we can cure about 40 percent of adult ALLs just because we used this principle, of using intensive therapy for a year. Now we treat it for two years so we can cure people. Treatments aren't specific enough to do it fast, because we're going down too slow, but it is, if you stay at it, you can cure them.

Tumor markers. Now that was a big breakthrough. And then of course when we came here, we started on AML and that's a different story. But all this went on at the Cancer Institute in ten years. First platelet transfusions, now universal practice, continuous flow blood cell separator, the whole field of chemotherapy, first multiple agent combination chemotherapy, the first early intensification, the first adjuvant therapy, the first claim of cure of systemic cancer. Ten years . . . basically.

And it was all because they were brave, heroic people and the regulators hadn't got after us yet. In 1997, none of this could be done in the United States. It's impossible.

GC: Too much regulation?

EF: Oh yes. It's psycho. We have a drug that I am certain—listen, no one has contributed more to the life of cancer patients, well maybe there are a few, maybe Zubrod, but I'm one of the ones who really has helped a lot of people. I know a lot about how to discover things. I've proven I can do it. It's like an Indy 500. If you build a machine that won fifteen races, someone come to you to build your machine, you'd be the one they'd beg.

But in this culture of ours, when I write a protocol, some twenty-year-old who has never done research, who's never discovered anything, who doesn't know how to count, who's making thirty-five thousand dollars a year, a GS-5, writes me a letter and says, "Freireich, you're stupid. You can't do it." That's the way we're organized. It's insane. The tables are inverted. That's all in the name of . . . .

You know, it's like any regulation. It's all in apparent good. It all came out of the thalidomide—I've written a chapter on regulation now. It's really a sad thing for this country. We have lost what the Clinical Center had. You know what war time did, it gave people lots of challenges and lots of opportunities and wealth and we've lost that.

We're now talking about cutting budgets and reducing health care. We can't afford health care. I hear these liberals saying, "We're spending 14 percent of the GDP in health care, we can't afford it, we're destroying the country." So I say, "Look. We have no problems with food, shelter, and safety. I mean what's next. If it isn't health, what is it? Is it toothpaste or airplanes or vacations? I mean come on. What if we spend 50 percent of the gross domestic product on health care?"

What's wrong with that? That's the most important problem we've got. People want to live. They want to be healthy. They want a predictable life. They don't want to die when they're ten years old. I'm a big advocate of health research. And secondly, we've got to get out of the notion that safety is more important than progress. The human condition requires what God gave us. We've got to use our imagination. We've got to imagine nirvana. All religions are based on whatever we can imagine our species can become.

It's not a question of just hanging onto where we are, you know. You don't have to worry about overpopulation and depression and regulation and safety. We've got to think of what the world could be. What we could do. What would you do if you could do anything? When I walked into the Clinical Center, "Freireich, what are you going to do if you can do anything?" "Well, let's do something!"

Something we've lost in this country is the challenge for our imaginations to be innovative and creative, and particularly in research, clinical research, it's terrible. Regulation is totally oppressive. It's got to be eliminated. And funding has to be regulated, too.

GC: Now, you went back to the NCI recently.

EF: Yes, I did a study. A very important study. That was the best year of my life, 1990. For two reasons: One, our family grew up there, two of our four children were born in Bethesda, three of them as a matter of fact. We had just been married. We got married in '53, '65, so we'd only been married, the first twelve years, very traumatic because Deanie worked, we were very poor, we had four children, we didn't have disposable diapers, everything was work, work, work. We didn't see each other two hours a week. I worked twenty hours a day. We lived a ten-minute walk from the Clinical Center. My life was totally involved in that place, and it still is, and this place.

Because when you . . . one thing people who do regulation and legislation, people who are removed from problems can't understand, administrators, is the impact of disease on human beings. I mean if you're a doctor, you've got . . . we have sixty leukemia patients in the hospital right now. Fifty of them are going to die in the next three months. And they're worried about whether this drug is going to be toxic? I mean, you know, come on.

It's like AIDS, we've got to do something about people like this. Leukemia should be solved. We should cure it and get on with it. We shouldn't worry about whether the drug is going to kill normal healthy people. We're not going to give it to normal healthy people. Anyway, and we shouldn't worry about money, research should be free, we shouldn't worry about budgets. It's the highest priority we've got. Once you get to defense and food and shelter, you know poverty, that's what matters. That's what people want to spend their money on.

I'm a big advocate of health research. I think we have to get on with it. Cancer should have been cured in our lifetime. We've got the principles. We know we can do it. Now we've just got to do the work. It's like I said about the platelets. Once I'd done the experiments in the lab, I knew we could do it. It's just now you've got to do it.

The same with the blood cells. Once you saw that you could do it, like going to the moon. Kennedy said, "Well, we think we've got it. Let's go." We know we can cure cancer. We should do it. But we've got to work on it. We've got to take bright young people with unlimited opportunities. It's going to take funding, it's going to take patients who are willing to participate. They do. We don't have any problem with that. We have patients coming in droves. What else can I tell you?

GC: When you went back to the NCI in 1990—

EF: It was deja vu. I enjoyed it very much.

GC:—what had changed? Was it completely different?

EF: Completely different. First of all, the NIH has been replicated across the country. The alumni have populated the academic institutions in the United States. So if you compare the Clinical Center 1990 to the M. D. Anderson 1990, it's [the Clinical Center] a primitive backward hospital. It should have been torn down a long time ago. In 1954, it was magnificent. In 1997, it's ridiculous. It's primitive, the construction is primitive, it's been patched up so many times it can barely stand. So their facilities were poor. If you go up to my hospital here—and we're building a new one because this one's out of date—I take care of patients in a dignified environment. Every patient has a private room, we have good facilities, good support people, we have an IV team. The Clinical Center practice is primitive.

[Interruption]

EF: Secondly, the clinical research atmosphere in this country has shifted away from the problem. The kinds of things that we did in the '50s first of all cannot be done because of regulations. So clinical research is boring. When Dr. Varmus and Dr. Klausner talk about clinical research, they're not talking about this kind of stuff. They're talking about whether you give methotrexate twice a day or once a day. They're talking about differences, whether you live a hundred days or two hundred days. Those are all applied problems. That's not clinical research, that's just office practice. There are no ideas. There's no challenge. There's no intellect. Clinical research is organized now—committees, groups. NCI has to be accountable to Congress, so everyone who wants to do research, me, I have to apply to some bureaucrat at the NCI. When he approves, it has to go to a bureaucrat at the FDA and if he approves it, God forbid it's original because it wouldn't have been done. They can't understand it anyway.

So there's an atmosphere of administration at the NIH now. They're overwhelmed with it. If you listen to Klausner, every time he talks, "We need more clinical research." What's he talking about? Well, I don't know what he's talking about, but he's not talking about the kind of things we do.

It's patient advocacy now. We have to work on breast cancer. Why do we have to work on breast cancer? Because women are dying of breast cancer. Oh, is that right? Well maybe we don't have any ideas on breast cancer and we want to work on leukemia, which is rare. Well, you don't want to work on leukemia, you've got to work on breast cancer. You've got to work on lung cancer. You've got to quit smoking. Patient advocacy.

Then we have "prevention is more important than cure." That's the one I like the best. That's my pet peeve. Bailar just wrote this great article in the *New England Journal*. One of the most important medical journals publishes an article by a statistician who claims that we should spend 60 percent of our research budget on cancer prevention. Brilliant thinking. Now you see, that's the thinking of someone who is in outer space, literally.

[Interruption]

EF: Think about it for a minute. We knew everything we needed to know to prevent the mortality from lung cancer in 1953. That was forty-five years ago. And lung cancer is still the leading cause of death from cancer in the United States. You know why cancer prevention is an illusion? Because people don't do what they're told.

People are still smoking. This is forty-five years. Now compare the prevention strategy for lung cancer to the curative strategy for choriocarcinoma, for childhood leukemia. Eighty-five percent of children with Hodgkin's disease are cured, 85 percent of children with leukemia are cured. How many lung cancers have we prevented after forty-five years having complete knowledge? Peanuts. It's silly.

Let's take diet. Diet causes colon cancer. Guess what? If you don't eat red meat for the rest of your life, you may get the colon cancer, incidence is now 10 percent. Okay. Now how are you going to implement that? Are you going to have a law against red meat or are people going to volunteer?

We're doing prevention studies where women have to take tamoxifen for twenty-five years. The trouble with prevention studies is so obvious. It is that the people who never need it are doing it. Do you understand? Everybody's not dying of cancer. But everybody has to prevent in order to prevent. It's healthy people who have to do it.

How do you get healthy people to do things that are bad for them? You can't get me to take tamoxifen for twenty years on the basis that I might prevent breast cancer. What are you talking about? The nice thing about treatment is the people involved are the ones who are motivated. When you're sick you go to the doctor. If you want to live, they'll all go to the doctor. Treatment always works. Secondly if you look at the history of medicine, there's been little progress that has been based on prevention. They're all treatment strategies. Treatment is the best prevention. So that's one of the big things.

Research has become political. It's not an idea, it's not an administrative intellectual activity any more. It's all political. Advocates. "We have to do prevention." I mean there's nothing intellectual about Bailar saying we should spend—you know *The Cancer Letter* asked him, "How did you figure 60 percent of the budget for prevention?" "Well, 60 percent seemed like a good number."

Any school boy could do that. Where's the brains? Where's the thinking? It doesn't exist. That's what's going on. The National Institutes of Health has become political. It's too public. Everybody's involved in all the decisions. For creativity you need just a few people, highly motivated, working hard, in an ideal environment. You can't discover things in the public arena. It's not a political event, discovery. So it's become too political.

Poor Broder who hired me and who's a wonderful, wonderful person . . . . You know Broder discovered something in his lifetime that affected AIDS patients. Are you going to talk to Broder?

GC: Yes. Next week.

EF: To his credit, DeVita discovered something. He saved lives. He was a real doctor at one point. Rosenberg discovered something. But you know Broder ended up getting canned over this stupid business with the groups and the breast cancer. That's the trouble, you see. When you're a bureaucrat you cannot afford to discover anything. It's just too dangerous.

[End Side A, Tape 2]

[Begin Side B, Tape 2]

EF: We did great things at the NIH and then everybody else wanted to do it. So they established the grants program. So now in order to run a grants program you've got a big administrative hoop-de-do. What is it, 85 percent of the dollars that go to NIH are spent in other institutions. This institution is NIH-supported basically. The consequence of that is that we don't have any freedom because NIH has to be responsible for everything we do so we get the money but of course what's the golden rule? Them that has the gold make the rules.

So we have to follow their rules. So the guys making the rules are just bureaucrats. So what's happened with the grant program is that we established peer review systems for these grant programs, the division of research grants, study sections. To make a long story short, the money that is allocated for research has progressively flowed into the basic sciences.

And it's reached the point where everybody at NIH is a basic scientist. Varmus does not see patients. Klausner does not see patients. He's director of the Cancer Institute. He doesn't know about cancer except what he reads in John Bailar's articles. That's a political job, and the consequence is that the leadership is not professional. They're not cancer doctors. That's what's lacking at the NIH.

When I was there, in 1990, I did a study of training for clinical investigators throughout the country. I traveled to the twenty leading cancer centers for training young physicians to become clinical investigators. I wrote a paper in which I showed that what's happening is that the clinical investigators are so oppressed that there are very few intelligent people going into that field.

The bright ones who enter clinical research all end up in laboratory research. Varmus, Klausner. You win the Nobel Prize, you get to be director of the Cancer Institute, not by taking care of patients and discovering how to cure cancer, but by cloning genes and discovering how Von Hippel-Lindau's disease is organized, and discovering how an oncogene works. Now Varmus and Klausner's discoveries are very, very important but whether they will ever help anybody is not clear.

We have to somehow do what the people who were over at the Clinical Center did. We have to have an era where physicians and patients can have an opportunity to engage in controlling disease by treatment. And they have to be unfettered by regulation, money. They have to have opportunity to be creative. We need another golden age of cancer research where you do what—When I went to the Clinical Center, they didn't say, "Freireich, you have to work on lung cancer because that's the commonest cancer." They said, "Do whatever you want." And we read the literature and said, "Hey, maybe we can do leukemia because there are some responses in leukemia. That's where the window is."

We didn't, like Bailar, sit back and say, "Prevention is better than cure." Which is false. I even have a book in which a Ph.D. did a study of whether prevention is ever better than cure. In the first place, you can't afford any prevention strategies.

What if we had—you know what happened after polio, when they discovered the vaccine to vaccinate children. Do you know the first years were total chaos because we didn't have enough money to vaccinate everybody against polio. I mean eventually it worked. But you know vaccination against polio, vaccination against smallpox, a great elimination of typhoid, all the great public health measures, they're all great. But those are all things based on external pathogens. The solution is obvious.

Cancer is not an external pathogen. Cancer is your own body turned against itself. It's a very complicated biology. We know a lot about biology and we have to restore to this enormous wealth of basic science knowledge.

Young physician scientists who are adventurous and innovative and that's the air we need in the Clinical Center. They're trying to do it. They have a program for young people who train there, but they all end up going into the laboratory. Now there's nothing wrong with going into the laboratory. I worked in the laboratory but I never gave up my clinical expertise. I always kept my eyes on the patients and I still do that.

GC: So you had a lot of daily contact with your patients.

EF: Every day. I still do. Every day. Those pages [on his beeper] I just got are my patients. There are four patients I have to see today, plus doing this [interview].

GC: You were talking for a minute about the leadership. Heller and Endicott were the directors you worked under. Is that right?

EF: Yes.

GC: What do you remember about them?

EF: Heller, he's a very nice man. Not significant. Endicott was a failed pathologist who had the insight not to tell people what to do and Zubrod was the leader. Endicott was a very nice person, but nothing significant as far as scientific leadership.

GC: Now did Heller and Endicott ever come to the Clinical Center?

EF: Not that I ever saw. Endicott was a pathologist for a while and he worked for Red Stewart. There were a lot of heroes that I dealt with. One of the things I discovered was meningeal leukemia, I worked with a guy named Louis B. Thomas. Are you going to interview him?

GC: He's someone Nancy Brun told me to ask you about.

EF: He's wonderful.

GC: Is he in Colorado?

EF:I don't know where he is actually. I think Kansas, but I'm not sure.

GC: Okay.

EF: You'll have trouble finding him, but he was a great guy. He worked for Red Stewart. Red Stewart's still there. Is he on your list?

GC: He's on my list. He hasn't agreed to an interview so far.

EF: He's a little cranky but he's terrific. Red Stewart was there, and Lou Thomas was a Red Stewart fan and we did a lot of work in pathology. My first important paper was a pathology paper I did with Lou Thomas. There's a big Zubrod anecdote there, too. I had two patients came to the clinic within a week of each other. Young, healthy adults who had very high blood counts and they were feeling completely well. It was discovered at a physical and they said, "Listen. I just want to take the weekend off with my wife." And they came in two days later dead of a stroke.

And that really impressed me so I called Lou and we got autopsy permission and we looked at their brains and we saw something funny. We saw lesions that we didn't normally see and we took out all the other people who had died and we looked at them and it was different. We wrote a paper where we described that patients with high white counts develop a unique kind of hemorrhage where the leukemic cells plug up the blood vessels. Since we were young and Zubrod was very anxious that we shouldn't publish things that are going to make us look bad, it was an experiment, we had an external advisory board and one of them on the committee was Dr. Farber, and Dr. Farber was like Dr. Keefer. He came to the Clinical Center and we were all in awe.

So Dr. Zubrod insisted that we present our data to Dr. Farber before we publish it, so we did and Dr. Farber—I remember it like it was today, we were in the auditorium and all my colleagues and professors and bosses were there—he got up and he said . . . . If you knew Dr. Farber, he was a magnificent person, just a very impressive guy, in all of his elements and he said, "You know—"

He was the big booster of the NIH Clinical Center. He was the one in the very last group that got a lot of money for us. "It's so wonderful to see these young people working so hard. I am really impressed. However, there is no relationship between the white count and the outcome. It's all wrong." We were crushed. We left the room, we went back and cried. Dr. Thomas and I went back over the brains, we went back over the counts, we looked at everything. We said, "I'm sorry. Dr. Farber's wrong."

So we wrote a paper and we sent it through. Dr. Mider said, "You cannot publish it. Dr. Farber says it's wrong." So we went to Dr. Zubrod, and Dr. Zubrod said, "Come on. Why don't you just study some more brains." Zubrod is not a confrontationalist. He's a diplomat. That's what made confrontational people like me possible, that he was there. He saved me from Mider all the time as I've explained to you.

Anyway, thanks to Frei, Frei is the one who got Zubrod to protect us. Dr. Thomas and I had a meeting and we looked at the paper again and we said, "You know, this is a matter of intellectual freedom, and we are not going to be oppressed. We're going to send it to the *Journal*. And we went to Zubrod and we told him we were going to do that. And he said, like he did with the platelets, he said, "It's not right, but it's your privilege."

So we did. And of course it's not only true, but it's been confirmed all the world over and it's one of the rules of treating leukemia. When the white count gets over fifty thousand, we'd panic because the vessels were beginning to sludge. You get leukostasis. Lou Thomas was the one. I couldn't have done it without him. He was another honest Kansas farmer who came from a poor background and he just wasn't going to be told what he thought was right was wrong. We did it. Those victories don't make you popular, I want you to know. People don't like being wrong in public. I did the same thing with Dameshek. I confronted him in public.

GC: Do you need to stop?

EF:I have a meeting at twelve. What are you doing? I want you to be happy.

GC: What am I doing? Let me pause the tape. I'll just make this the last question because I know you don't have much time. I wanted to ask you about the teamwork you did. How did you work together as a team with Frei and Louis Thomas and all those people? Did one person come up with an idea and then other people would build on it? How would things go when an inspiration came to one of you?

EF: As I say, we had the advantage of, the analogy I use is battlefields. When you're in a war, when your life is threatened and you're in a foxhole, the teamwork is automatic. The same thing happens in crisis situations. You know when a plane falls down on top of the Andes, the first thing people do is they look at each other and say, "If we're going to make it, we've got to get organized. You're the doctor. You go forage for food." Someone who is a natural leader emerges. That's the way it goes.

We had an enormously safe, big opportunity, but it was very threatening, accused of experimenting on people, ruining the whole concept was very large and looming all the time. We had to succeed. So we had an alliance that is forged under fire. That is, people moved in the directions that they could go. Frei recognized a good relationship with Zubrod. He realized that I was a confrontational type right away, and he could take it. He was one of those people who could take it. So we had a natural flow of authority that functioned well.

Frei never did anything he'd thought was wrong, but he's very open-minded so when something that flew in the face of what he thought was right was there, he'd listen and think about it. Zubrod had a similar orientation. But the main thing that brought people together was motivation. It's <u>wanting</u> to know the answer. Lou Thomas and I were Sunday morning, he was a religious guy, he gave up church to come into the morgue and look at those brains. We just had to know, and we both wanted to know. So we did it together.

It's like when we published our paper, we just had to get it out. Those kinds of collegialities are stronger than the bonds you make with family because those are very trying moments. Pressures are high and motivations high, opportunities high, rewards are big. People always ask you what the secret of success is. I say there's only two things. You don't have to have any ability. You just need motivation and opportunity.

If America wants to cure cancer, that's what we need. Motivated people and give them the opportunity. They're here. People are innately motivated. Nobody likes to be lazy and sit around and do nothing. Everybody wants to be significant. That's why we have religion. Everybody wants to feel that what they did in their lifetime was something that they left. Something for our species, for the world, for the future. Everybody's motivated.

But it gets kicked out of you. A couple of failures early on, first thing you know you're a drone. So the motivation is there. What we have to do is the successful and powerful people have to create opportunity. That's what the Public Health Service did for me. That's what Armstrong did for me. That's what Cook County did for me. That's what my physics professor did for me. They just said, "Okay, here's someone. Give him a chance. Go to college. Here's someone. Give him a chance. Let him go do research in a laboratory." But other people have to do it.

When I go back to Illinois, when I got my honorary degree I had to give a speech, and I said, "I belong to the taxpayers of the state of Illinois." The University of Illinois, tax-supported, Cook County scholarship, rehabilitation program, that's how I got to be a doctor. Just given the opportunity.

That's the solution to the poverty problem, you know. You can't give people money to be doles. You've got to work out a system that gives them opportunity. It can't be easy. I happen to be arch right-wing as you might imagine because I really believe that what makes humans human is motivation. They've got to want to do some good. They've got to grow up in environments where doing good—my parents, my mother was very fundamentalist and my sister was very fundamentalist. They wanted to do some good, they wanted me to do some good. The community I was in, very fundamentalist. People wanted to succeed, get out of the ghetto. Motivation and opportunity.

It's a good job. Hope you'll succeed.

GC: Thank you. This ends the tape with Dr. Freireich.

[End of interview]

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